

### **REMARKS/ARGUMENTS**

Reconsideration of this application is requested. Claims 1-14, 16 and 17 are pending in the application subsequent to entry of this Amendment.

The claims have been amended in order to more particularly point out and distinctly claim that which applicants regard as their invention and for purposes of clarity in particular responding to item 2 of the current Official Action.

In claim 11 the examiner has objected to the term "high concentration". To resolve this concern the subject matter of claim 15, which states a definite concentration, has been incorporated into claim 11 and claim 15 has been canceled as being redundant.

The examiner considers the outer range of 10  $\mu$ m in claim 12 to be inconsistent with the term "submicron" as used in claim 1. Applicants disagree and believe that the terminology employed in claim 12 is appropriate and consistent with current understanding and practice.

In the preparation of liposomes, it is impossible to make all the liposome particles having an identical size, thus there must be a profile of a *Poission* distribution in the particle diameter of the liposomes. When determining the average diameter of the liposome of the present invention using, for example, DLS, the average diameter is certainly submicron in size. However, the upper limit in the diameter range of the submicron liposome is around 10  $\mu$ m. This can be easily understood by a person skilled in the art of liposome preparation.

The expression centella asiatica extract has been deleted from claim 13.

In claim 17, the term "pack" may also be referred to as a "mask" and with this equivalency in mind claim 17 has been adjusted for purposes of clarity.

In preparing this response various grammatical changes were made in claims 1, 5, 9, 12, 14 and 17.

It is respectfully submitted that the changes made to the claims are based upon the original description of the invention and that added subject matter is not involved. The claims are believed to be consistent with the requirements of 35 USC §112, second paragraph. Reconsideration and favorable action are solicited.

The Official Action includes three separate prior art-based rejections of alleged "obviousness": *see* items 4-6. Applicants consider the process employed in the present invention as fundamentally distinct from the disclosures of all of these documents and in

particular U.S. patent 5,716,638 to Touitou, the primary reference in each of these three rejections.

The object of the present invention is to provide submicron liposomes containing triterpenoid at a high concentration while using a non-toxic solvent without intensive mechanical treatment. In order to incorporate the triterpenoid at a high concentration uniformly into a liposome, the present invention employs a triterpenoid having acid group, and by adding a base, the triterpenoid is transformed into its salt having surface activity.

The transformed triterpenoid salt is a surfactant of a high HLB, and it forms a mixed micelle system when mixed with a low HLB lipid. The above-obtained mixed micelle system maintains its pH in a range of 10~11. By adding an acid to decrease its pH to 5-8, the triterpenoid salt reverts back to its original form having an acid group, and thereby loses its surface activity, thereby changing the mixed micelle system into a liposome. During the transformation, the triterpenoid is loaded into the liposome at a high concentration. (See page 2, third full paragraph of specification of the present invention.)

None of the cited documents disclose such use of an acid and a base for transformation into a mixed micelle system or liposome as in the present invention. Thus, the present invention is considered to be non-obvious over the teachings of the cited documents.

For the above reasons it is respectfully submitted that the claims of this application define inventive subject matter. Reconsideration and allowance are solicited.

Respectfully submitted,

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